

REMARKS

Upon entry of the amendments made herein claims 10-17, 22-31, and 38 are pending in the application. Claims 1-9, 18-21, 32-37, and 39 are canceled. Applicants reserve the right to prosecute the subject matter of these claims in one or more continuing applications. Claims 10-17, 22-29, and 31 are amended to properly depend from claim 38. No new matter has been added.

Objection to the Specification

The Examiner has objected to the title of the invention as it is not descriptive. The title has been amended to read “ Method of Treating Cancers using β -lapachone or Analogs or Derivatives Thereof,” which is indicative of the invention in view of Applicants’ Response to the Restriction Requirement. As such, Applicants request reconsideration and withdrawal of the objection.

35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 4, 6 and 7 under 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 4, 6, and 7 are canceled. Therefore, this rejection is moot and should be withdrawn.

35 U.S.C. § 112, First Paragraph

Written Description

Claims 1-7, 9-31 and 36-38 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art, that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically the Examiner states that the specification disclosed specific cell cycle checkpoint activators, including β -lapachone, and

specific oncogenic kinase modulators, including imatinib, which meet the written description requirement, however, the “derivatives or analogs” of β -lapachone or undisclosed oncogenic kinase modulator/cell cycle checkpoint activator, do not meet the requirement because there is a lack of chemical structure information for what they are and the chemical structures are highly variant and encompass a myriad of possibilities. *See*, Office Action at pages 10 - 12.

Claims 1-7, 9, 18-21, and 32-37 are canceled. Claims 10-17 and 22-31 are amended to properly depend from claim 38. Claim 38 is specifically drafted to a method of treating multiple myeloma or chronic myelogenous leukemia comprising administering a therapeutically effective amount of β -lapachone or a derivative or analog thereof and imatinib. Applicants traverse the rejection with respect to the claims as amended herein.

Applicants submit that the present invention fully describes β -lapachone, as well as derivatives or analogs thereof. Specifically, the instant specification discloses β -lapachone derivatives and analogs, including essential chemical structural information, throughout the specification, for example, from page 18, line 9, to page 25, line 2. As such, Applicants submit that one of ordinary skill in the art would readily recognize that Applicants were in possession of the claimed invention at the time of filing. Reconsideration and withdrawal are respectfully requested.

Enablement

Claims 1-7, 9-31 and 36-38 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of treating multiple myeloma and chronic myelogenous leukemia comprising administering a therapeutically effective amount of β -lapachone in combination with imatinib or paclitaxel, does not reasonable provide enablement for methods of treating all cancers in a subject comprising administering any cell cycle checkpoint activator and any oncogenic kinase modulator. *See*, Office Action at pages 4 -10.

Claims 1-7, 9, 18-21, and 32-37 are canceled. Claims 10-17 and 22-31 are amended to properly depend from claim 38. Claim 38 is drawn specifically to a method of treating multiple myeloma or chronic myelogenous leukemia comprising administering a therapeutically effective

amount of β -lapachone or a derivative or analog thereof, and imatinib. Applicants traverse the rejection with respect to the claims as amended.

As described *supra*, the instant specification readily discloses β -lapachone and analogs and derivatives including essential structural information, for example, at page 18, line 9, to page 25, line 2. More specifically, the specification discloses a concise number of chemical formulae from which a defined plurality of β -lapachone analogs and derivatives are generated, beginning on page 21 (Formulas I and II), page 22 (Formulas III and IV), page 23 (Formulas V and VI), and ending on page 24 (Formula VII). The specification discloses that these compounds are G1/S phase cell cycle activators and Examples 1 and 2 provide working examples of the efficacy of β -lapachone and/or imatinib on cell lines derived from human hematological tumors (pages 28-31 of the specification). Additionally, methods for making solutions containing the appropriate concentrations of β -lapachone and analogs and derivatives thereof and/or imatinib, cell culture techniques, cell survival assessment, and evaluation/interpretation of the data are well-described throughout the specification. As such, Applicants submit that one of ordinary skill in the art would be able to make and use the invention as claimed herein without undue experimentation. Reconsideration and withdrawal is respectfully requested.

35 U.S.C. §103(a)

Claims 1-7, 9-18 and 29-31 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,070,797 to Pardee ("Pardee '797") in view of Topaly et al., Leukemia 15:342-347, 2001 ("Topaly").

Claims 1-7, 9, and 18 are canceled. Claims 10-17 and 29-31 are amended to properly depend from claim 38, which is not subject to the instant rejection. Thus, the rejection is moot and should be withdrawn.

Claims 19-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pardee '797, in view of Topaly, further in view of US Patent No. 6,664,288 to Pardee ("Pardee '288"), and in further view of US Patent No. 6,998,391 to Lyons ("Lyons").

Claims 19-21 are canceled. Claims 22-28 are amended to properly depend from claim 38, which is not subject to the instant rejection. Thus, the rejection is moot and should be withdrawn.

Nonstatutory Obviousness-Type Double Patenting

Claims 1-3, 7, 9-21, and 23-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 3-13, 15-40, 42, 45-48, and 50-51 of Pardee '797, in view of Topaly, in further view of Pardee '288, and further in view of Lyons.

Claims 1-9 and 18-21 are canceled. Claims 10-17 and 23-31 are amended to properly depend from claim 38, which is not subject to the rejection. Thus, the rejection is moot and should be withdrawn.

Claims 1-7, 9-31, and 38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of Pardee '288, in view of Pardee '797, in view of Topaly, and further in view of Lyons.

Claims 1-9 and 18-21 are canceled. Claims 10-17 and 22-31 are amended to properly depend from claim 38. Claim 38 is drawn to “a method of treating multiple myeloma or chronic myelogenous leukemia in a human, a method comprising administering to the subject a therapeutically effective amount of β -lapachone or a derivative or analog thereof, and imatinib, such that the multiple myeloma or chronic myelogenous leukemia is treated.” Applicants traverse with respect to claims 10-17 and 22-31 as amended herein.

To be a proper rejection on the ground of nonstatutory obviousness-type double patenting, the Examiner must make clear the differences between the inventions defined by the conflicting claims (*i.e.*, claims 1-10 of Pardee '288 and the pending claims as amended herein) and make clear the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claims at issue would have been an obvious variation of the claims 1-10 of Pardee '288. *See*, M.P.E.P. at § 804. Applicants submit that the Examiner has failed to meet this burden and has failed to provide any evidence to support the instant rejection.

Claim 1 of Pardee '288 (from which the remaining claims depend) is drawn to “a

method of treating a mammal having a solid tumor (or tumors) formed as a result of a cancer selected from the group consisting of melanoma, colon cancer, prostate cancer, lung cancer, pancreatic cancer, ovarian cancer and breast cancer, the method comprising: a) administering to a mammal an effective amount of a compound comprising β -lapachone or derivatives thereof as the active ingredient; and b) administering to the mammal an effective amount of a G2/M phase drug.”

Pardee ‘288 does not teach or suggest treating multiple myeloma or chronic myelogenous leukemia. Pardee ‘288 does not teach or suggest the use of imatinib, alone or in combination with β -lapachone or derivatives thereof, to treat multiple myeloma or chronic myelogenous leukemia. Pardee ‘797, Topaly, and Lyons do not cure these deficiencies of Pardee ‘288.

While Pardee ‘797 does teach the treatment of multiple myeloma with the combination of β -lapachone or derivatives thereof and taxol derivatives; similar to Pardee ‘288, Pardee ‘797 does not teach or suggest the use of imatinib, alone or in combination with β -lapachone or derivatives thereof, to treat multiple myeloma or chronic myelogenous leukemia.

Topaly merely teaches the treatment of BCR-ABL-positive chronic myelogenous leukemia (CML) cells by combining imatinib with mafosfamide, hydroxyurea, cytarabine and etoposide. Topaly does not teach or suggest β -lapachone or derivatives thereof. Further, Topaly does not teach or suggest the use of imatinib, alone or in combination with β -lapachone or derivatives thereof, to treat multiple myeloma or chronic myelogenous leukemia.

Lyons merely teaches the treatment of leukemia with a combination of decitabine and a tyrosine kinase inhibitor. Lyons does not teach or suggest β -lapachone or derivatives thereof. Lyons also does not teach or suggest imatinib. Further, Lyons does not teach or suggest the use of imatinib, alone or in combination with β -lapachone or derivatives thereof, to treat multiple myeloma or chronic myelogenous leukemia.

One of ordinary skill in the art reading Pardee ‘288, Pardee ‘797, Topaly, and Lyons would not be motivated to combine these references to reach the present invention.

The Examiner's sole reasoning for the instant rejection is that since Pardee '797 teaches that treating multiple myeloma with β -lapachone and paclitaxel is effective and synergistic, and thus one of ordinary skill in the art would be motivated to treat multiple myeloma or chronic myelogenous leukemia with the combination of β -lapachone and imatinib, as claimed herein, with a reasonable expectation of success. The Examiner has provided no evidence to support this reasoning. Further, Applicants wish to point out to the Examiner that it is claims 1-10 of Pardee '288 which are subject to the instant rejection and not the claims of Pardee '797. The Examiner has provided no nexus for comparing the disclosure of Pardee '797 which describe the treatment of multiple myeloma with β -lapachone and paclitaxel with the claims 1-10 of Pardee '288 which are directed to treating a mammal having a solid tumor (or tumors) formed as a result of a cancer selected from the group consisting of melanoma, colon cancer, prostate cancer, lung cancer, pancreatic cancer, ovarian cancer and breast cancer with a combination of β -lapachone and a G2/M phase drug. This is clearly a rejection based on an obvious-to-try standard which is not permitted.

In some cases, what would have been obvious to try would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.... In others, what was obvious to try was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it (Emphasis Added). *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

As such, Applicants submit that pending claim 38, from which the remaining claims subject to the rejection properly depend, are patentably distinct from claims 1-10 of Pardee '288. Reconsideration and withdrawal is respectfully requested.

Claims 1-7, 9-31, and 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-26, 30-31, 34-38, 40-46,

50-51, 55-58, 60-64, 94-95, 101-105, 107-111 of copending US Patent Application No. 10/007,352.

US Patent Application No. 10/007,352 is abandoned. Thus, this rejection is moot and should be withdrawn.

Claims 1-7, 9-31, and 36-38 are provisionally rejected as allegedly being unpatentable on the ground of nonstatutory obviousness-type double patenting in view of US Patent Application No. 10/846,980. Applicants note that this is a provisional double patenting rejection for which the M.P.E.P. at § 1504.06 Double Patenting provides as follows:

If a provisional double patenting rejection (of any type) is the only rejection remaining in two conflicting applications, the examiner should withdraw that rejection in one of the applications (e.g., the application with the earlier filing date) and permit the application to issue as a patent. The examiner should maintain the provisional double patenting rejection in the other application which rejection will be converted into a double patenting rejection when the first application issues as a patent. If more than two applications conflict with each other and one is allowed, the remaining applications should be cross rejected against the others as well as the allowed application. For this type of rejection to be appropriate, there must be either at least one inventor in common, or a common assignee. If the claims in copending design applications or a design patent and design applications have a common assignee but different inventive entities, rejections under 35 U.S.C. 102(e), (f) and (g)/103(a) must be considered in addition to the double patenting rejection. See MPEP Section 804, Section 2136, Section 2137 and Section 2138.

Accordingly, should the Examiner find the present claims allowable in view of the above amendments and/or arguments, Applicants respectfully request withdrawal of this provisional rejection.

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Applicant(s): Li *et al.*

CONCLUSION

On the basis of the foregoing amendment and remark, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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